REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. Claims 1-112 are pending in the instant application, and claims 58-74 are currently under consideration. Claims 58, 60, 64, and 70-72 have been amended, and claims 1-57, 59, 61-63, and 75-112 have been canceled. Support for these amendments may be found throughout the specification (*e.g.*, at page 18, lines 1-24; pate 45, line 6 through page 46, line 12; pages 92-112) and claims as originally filed, and it is urged that the amendments do not constitute new matter. It should also be noted that the above amendments are not to be construed as acquiescence with regard to the PTO's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

RESPONSE TO RESTRICTION REQUIREMENT

In response to the restriction requirement, Applicants hereby elect Group VII, claims 58-74, drawn to a method of determining the presence of an ANT polypeptide in a sample, classified in class 435, subclass 7.1, for examination at this time.

OBJECTION TO THE DISCLOSURE

The Action objects to the disclosure for allegedly containing informalities by not providing sequence identifiers for the sequences listed in Figures 1A, 1B, and 2.

Applicants have amended the Brief Description of the Drawings to reference the appropriate sequence identifiers, as indicated above. Applicants respectfully request that this objection be withdrawn in light of the present amendment.

OBJECTION TO THE CLAIMS

The Action objects to claims 58 and 72 for allegedly containing informalities in not providing the full name of the polypeptide referred to by its acronym, "ANT."

Applicants have amended claims 58 and 72 to recite the full name of the polypeptide, "adenine nucleotide translocator." Applicants respectfully request that this basis of objection be withdrawn in light of this amendment.

REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 59 stands rejected under 35 U.S.C. § 112, second paragraph, for reciting an element, "the adenine nucleotide translocator polypeptide", that allegedly lacks antecedent basis in claim 58. Applicants have canceled claim 59 and amended claim 58 to recite "an adenine nucleotide translocator polypeptide," thereby providing antecedent basis for the recitation in claim 59 and obviating this rejection. Applicants respectfully request that this basis of rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 60-62 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. More specifically, the PTO asserts that claims 60, 61 and 62 are drawn to methods of determining the presence of, respectively, ANT1, ANT2, and ANT3 polypeptides in a sample, alleging that undue experimentation would be required to practice the invention where the claimed methods do not include any steps that would allow differentiation between these different ANT isoforms.

Applicants respectfully traverse this rejection and submit that the methods of claims 60-62 are fully enabled by the instant specification. However, solely to expedite prosecution and without acquiescence in this rejection, Applicants have canceled claims 61 and 62 and amended claim 60 to recite that the claimed methods are directed to determining the presence of one or more of human ANT1, ANT2, or ANT3. Applicants submit that the skilled artisan would appreciate that, as amended, claim 60 relates to detection of any one or more of the recited ANT polypeptides, *i.e.*, human ANT1, human ANT2 or human ANT3. In view of these amendments and remarks, Applicants respectfully request that this rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 58, 63-66, 71, and 72 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Schultheiss *et al.* (1983 *Clin. Exp. Immunol.* 54:648). More specifically, the Action asserts that Schultheiss *et al.* teach a method of determining the presence of an ANT in

bovine mitochondria samples comprising contacting samples with radiolabeled carboxyatractyloside, an atracyloside derivative.

Claims 58, 63-66, 70, and 72-73 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Brandolin *et al.* (1974 *FEBS Lett.* 46:149). Specifically, the Action asserts that Brandolin *et al.* teach a method for isolating an ANT by contacting rat liver mitochondria with succinyl-atractyloside-amino Sepharose, an atracyloside derivative, and recovering the ANT using radiolabeled atractyloside.

Claims 58, 63, 70, 72, and 73 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Bojanovski et al. (1976 *Eur. J. Bioch.* 71:539). Specifically, the Action asserts that Bojanovski *et al.* teach a method for isolating ANT by contacting rat liver mitochondria with carboxyatractyloside, an atracyloside derivative.

Claims 58, 63-66, and 71-72 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Klingenberg *et al.* (1978 *Biochim. Biophys. Acta* 503:193). Specifically, the Action asserts that Klingenberg *et al.* teach a method of isolating ANT by contacting beef heart mitochondria with radiolabeled carboxyatractyloside, an atracyloside derivative.

Applicants respectfully traverse these bases of rejection and submit that the instant claims are not anticipated by any of these references. Applicants note that claims 58 and 72, as amended herewith without acquiescence to any rejection of record, are expressly directed to methods of determining the presence of or isolating a human ANT polypeptide. Support for this amendment is provided throughout the specification as originally filed, including, *e.g.*, at page 9, lines 9-10.

It is axiomatic that for a cited item from the prior art to anticipate a claimed invention, each and every feature of the invention must be disclosed in a single reference from the prior art. Since none of the cited publications describes a method related to determining the presence of, or to isolating, a human ANT polypeptide, these documents fail to describe each and every element of the instant claims. Accordingly, the PTO fails to establish a *prima facie* case of anticipation of the claimed invention. Applicants therefore respectfully request that these rejections be withdrawn in light of the present amendments and the foregoing remarks.

REJECTION UNDER 35 U.S.C. § 103

Claim 59 stands rejected under 35 U.S.C. § 103(a) as allegedly obvious over Schultheiss *et al.* (1983 *Clin. Exp. Immunol.* 54:648) in view of Fiore *et al.* (1998 *Biochimie* 80:137). More specifically, the PTO asserts that Schultheiss *et al.* teach a method of determining the presence of an ANT in bovine mitochondria samples comprising contacting samples with radiolabeled carboxyatractyloside, an atracyloside derivative. The Action concedes that Schultheiss *et al.* fail to teach methods of detecting a human ANT, but alleges that Fiore *et al.* remedy this deficiency by teaching the sequence of three isoforms of human ANT. Applicants respectfully point out that claim 59 has been canceled by the amendment submitted herewith, thereby rendering this rejection moot.

Claims 67-69 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over Schultheiss *et al.* in view of Fiore *et al.*, Rosenberg (1996 Protein Analysis and Purification: Benchtop Techniques, Birkhauser, Boston, pp. 170-82 and 303-322), and Osman *et al.* (1993 *J. Immunol. Meth.* 161:97). The PTO alleges that Schultheiss *et al.* teach a method of determining the presence of an ANT in bovine mitochondria samples comprising contacting samples with radiolabeled carboxyatractyloside, an atracyloside derivative, but concedes that Schultheiss *et al.* do not teach the use of a fluorescently labeled atractyloside. Rather, the PTO asserts that Fiore *et al.* suggest the use of fluorescently labeled atractyloside to detect ANT, and that Rosenberg teaches that radiolabeling and fluorescently labeling a ligand of a protein of interest are functionally equivalent means for detecting proteins. Furthermore, the PTO asserts that Osman *et al.* teach that use of the Eu3+ fluorophore is functionally equivalent to other detection systems, such as biotin, radiolabeling, and other fluorescent labels. The PTO then asserts that it would have been obvious to modify the method of Schultheiss *et al.* by using a fluorescently labeled atractyloside derivative as suggested by Fiore *et al.*, and that the skilled artisan would have been motivated to use a fluorescent label because it had higher sensitivity.

Applicants respectfully traverse these grounds for rejection and submit that the cited publications, alone or in combination, fail to teach or suggest each element of the claimed invention and, therefore, that the PTO fails to establish a *prima facie* case of obviousness. Collectively or individually, Schultheiss *et al.*, Fiore *et al.*, Rosenberg, and Osman *et al.* all fail

to teach or suggest any use of an atractyloside that is substituted at the 6' hydroxy position, or of an atractyloside derivative that is substituted at 6' hydroxy, in a method for determining the presence of a human ANT polypeptide. As described in the instant specification, for example, at pages 45-46 and 92-112, the previously unrecognized substitution of atractyloside at 6' hydroxy permits modifications of atractyloside (ATR) that do not significantly alter ATR binding affinity for ANT, while affording opportunities for introducing into ATR a variety of substituents, including detectable moieties that can be introduced under mild conditions.

Schultheiss *et al.* merely describe carboxyatractyloside, a known atractyloside derivative that retains the 6' hydroxyl group and that is not substituted at 6' hydroxyl. Carboxyatractyloside is in fact recognized in the instant specification (*e.g.,* at page 44, lines 28-29), rendering Schultheiss *et al.* a merely cumulative disclosure. Similarly, Fiore *et al.* refer generally to the promise of fluorescence techniques for characterizing ANT, and specifically to naphthoyl-ATR and methylanthranyloyl-ATR, but none of these disclosures constitutes an express description of a 6' hydroxy substituted ATR derivative, nor can any document cited by the PTO reasonably be understood by a person having ordinary skill in the art in any way to suggest the use of an atractyloside that is substituted at 6' hydroxyl in the presently claimed methods.

Accordingly, and in view of the present amendment, Applicants submit that the application satisfies all requirements of 35 U.S.C. §103 and respectfully request that these rejections be withdrawn.

Additionally, applicants wish to call the Examiner's attention to several related co-pending applications having claims potentially directed to similar subject matter. Reference to the appended "Table of Co-Pending Applications" is therefore requested.

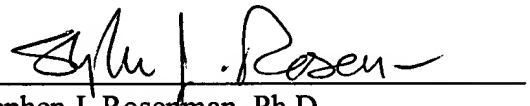
The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants submit that the claims remaining in the application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Christen M. Anderson et al.

SEED Intellectual Property Law Group PLLC



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APPENDIX: TABLE OF CO-PENDING APPLICATIONS

U.S.A.N.	Atty. Docket No.	Examiner	Claims directed to ____ (Comments)
09/393,441	660088.420C1	Sheridan Snedden	__ isolated recombinant huANT3 polypeptide that localizes to mitochondrial membrane Statutory double-patenting rejection of claims 42, 46-48, 51 and 57 over claims 42, 46-48,51 and 57 of 09/185,904
09/185,904	660088.420	Holly G. Schnizer	__ isolated recombinant huANT3 polypeptide Obviousness-type double patenting rejection of claims 42, 46-50 over claims 42, 46-48, 51 and 57 of 09/393,441
09/811,131	660088.420D1	Holly G. Schnizer	__ method of identifying agent that binds to ANT polypeptide
09/811,185	660088.420D2	Rebecca L. Anderson	__ method of treatment using ANT ligand
09/810,644	660088.420D3	Rebecca L. Anderson	__ ANT ligand
09/811,094	660088.420D4	Holly G. Schnizer	__ recombinant expression construct, host cell, and method of making recombinant ANT polypeptides and fusion proteins
09/811,132 (present application)	660088.420D5	Holly G. Schnizer	__ methods of detecting and isolating an ANT polypeptide, using ANT ligand
09/809,827	660088.420D6	Holly G. Schnizer	__ isolated recombinant huANT1 polypeptide
09/809,889	660088.420D7	Holly G. Schnizer	__ isolated recombinant huANT2 polypeptide
09/569,327	660088.443	Sheridan Snedden	__ method of producing recombinant ANT polypeptides and fusion proteins using tightly regulated promoter
10/684,232	660088.433C2	(none assigned)	__ANT-energy transfer peptide fusion proteins